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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER
BROWN, TIMOTHY M

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,883	EMINI ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 25-39* is/are pending in the application.

4a) Of the above claim(s) *3,9,18,19,21,27,31-33 and 37-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10-17,20,25,26,28-30 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see Detailed Actio*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received August 21, 2003, and the telephonic interview of December 9, 2005. Claims 1, 2, 4-8, 10-17, 20, 25, 26, 28-30 and 34-36 are under examination. Claims 3, 9, 18, 19, 21, 27, 31-33 and 37-39 are withdrawn. Claims 22-24 have been canceled.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Anna L. Cocuzzo on December 9, 2003.

In the claims:

Cancel claims 22-24.

Elections/Restrictions

The Examiner thanks Anna L. Cocuzzo for making an election (without traverse) of Group I, Species i, during a telephonic interview on December 9, 2005. The claims were subject to the following restriction:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, 4-8, 10-17, 20, 22-26, 28-30 and 34-36, drawn to a recombinant serotype 24 adenovirus vector which is at least partially deleted in E1 and devoid

of E1 activity, and a population of cells transformed with said vector, classified in class 435, subclass 235.1.

II. Claims 3, 9 and 27, drawn to a method for producing recombinant, replication defective adenovirus particles, class 435, subclass 325.

III. Claims 18, 19, 21, 31-33 and 37-39, drawn to a method for effecting the delivery and expression of heterologous nucleic acid, classified in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). Here, the adenovirus of Invention I can be administered to a subject as a vaccine. Thus, the product of Invention I can be used in a materially different process.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process (MPEP § 806.05(h)). Here, the method of Invention III is drawn to effecting the delivery and expression of a heterologous nucleic acid using a recombinant adenovirus vector. The delivery and expression of a heterologous nucleic acid may be achieved using naked DNA. Thus, the process of Invention III can be practiced with a materially different product.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Here, the objective of Invention II is the production of recombinant adenovirus. The objective of Invention III in contrast is to express a heterologous nucleic acid in a subject. Thus, Inventions II and III are unrelated due to different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

An election of Invention I requires a further election of one of the following species of HIV peptide:

i. gag

ii. nef

iii. pol

These species are patentably distinct because they are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Here, Species i-iii are drawn to HIV polypeptides having distinct chemical compositions and distinct biological activities. Therefore, Species i-iii are unrelated due to different effects.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Information Disclosure

The Information Disclosure Statements filed on the following dates have been considered, signed and attached to this Office Action: April 12, 2004; July 19, 2004; and May 9, 2005.

Claim Objections

Claim 7 is objected to for being ungrammatical. Amending the claim to recite "comprises a heterologous nucleic acid . . . ." would overcome this objection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4-8, 10, 12, 15-17, 20, 25, 26, 28-30 are provisionally rejected on the ground of nonstatutory double patenting over claims 43, 44, 46-48, 51 and 53 ("the co-pending claims) of copending Application No. 10/645,794. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. The claims are rejected because both applications are drawn to a recombinant adenoviral vector of serotype 24 which (i) is devoid of E1 activity, (ii) comprises a heterologous nucleic acid sequence that encodes an antigenic HIV-1 gag peptide.

Claim Rejections - 35 U.S.C. 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8, 10-17, 20, 25, 26, 28-30 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7 and 25 are indefinite for reciting "[a] recombinant adenoviral vector of serotype 24." This language is indefinite because it would not allow one skilled in the art to determine whether Applicants' recombinant adenoviral vector is (i) recombinant because it is type 24 adenovirus that comprises an E1 deletion, or (ii) recombinant because it comprises a type 24 adenovirus that comprises an E1 deletion and a heterologous nucleic acid.

Claims 1, 7 and 25 are indefinite for reciting "devoid of E1 activity." This language does not distinctly claim the invention because it is unclear which activities are lacking. For example, one skilled in the art would not be able to determine which of the many different E1A and E1B activities that "devoid of E1 activity" refers to.

Claims 1, 7, 14 and 25 are indefinite for reciting "at least partially deleted in E1 . . . ." This language does not allow one skilled in the art to determine whether the claims actually require a deletion in the E1 region. Amending the claims "[a] recombinant type 24 adenoviral vector wherein the vector comprises an E1 deletion . . ." is suggested. Claims 34-36 are indefinite for reciting "an immunologically relevant modification thereof." This language would not allow one skilled in the art to determine the scope of potential genetic modifications that are "immunoligically relevant."

Claims 34-36 are also indefinite because each of these claims lacks antecedent basis for "the HIV antigen."

Claim 12 is indefinite in the recitation of "codons optimized for the expression in a human host." This fails to point out with particularity the nature of Applicants' codon modifications.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-8, 10-17, 20, 25, 26, 28-30 and 34-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While the specification enables producing (i) recombinant serotype 24 adenoviral *replicons*, and (ii) recombinant serotype 24 *viral particles* comprising an Ad5 ORF6 region, it does not enable producing them as recombinant viral particles.

Applicants specification enables two general embodiments of the claimed adenoviral vector. First, the specification enables a recombinant type 24 adenoviral vector comprising an inactivating E1 deletion, wherein the adenoviral vector is a *replicon*. Second, the specification enables a recombinant E1-minus type 24 adenoviral vector wherein the vector includes a type 5 adenovirus ORF6, and wherein the vector is a *viral particle*. Practicing the other claimed embodiments of Applicants' adenoviral vector would however require undue experimentation.

Undue experimentation is defined by the following factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of

predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

Here, the claims provide that the recombinant adenoviral particle is "of serotype 24" and is "devoid of E1 activity." Thus, the breadth of the claims provides that the adenoviral vector may comprise type 24 adenovirus (Ad24) wherein the E1 activity of the virus has been destroyed by deletion or substitution with a heterologous nucleic acid sequence. Thus, the nature of the invention is a type 24 adenoviral vector that comprises an E1 attenuating mutation.

The state of the art at the time this application was filed taught little about the transfection efficiencies of Ad24, or the mutations that result in attenutation. Even less was known about how to obtain attenuated Ad24 particles using an E1-complimenting cell line. Thus, one skilled in the art could not possibly predict how producing E1-minus Ad24 in complimenting cell line would work. Making and using the invention would therefore require the skilled artisan to turn to the specification for directions on how to make and use Applicants' E1-attenuated Ad24 particles. The specification however only teaches producing the Ad24 replicons. There is insufficient direction in the specification to make Ad24 viral particles using a complimenting cell line. The specification teaches that deleting the E1 activity of Ad24 destroys the ability of Ad24 to form viral particles in PER-C6 cells. The specification further teaches that the replication of Ad24 may be rescued by inserting ORF6 from adenovirus type 5 (Ad5). Thus, the amount of direction provided by the specification would not enable one skilled in the art to make and use Ad24 viral particles that lack E1 activity unless the viral particles further comprise a Ad5 ORF6 to rescue replication.

It should also be noted that the specification fails to enable an Ad24 viral particle comprising a heterologous nucleic acid that has been substituted for a portion of the E1 genome. The specification fails to provide directions or a working example that would allow the skilled artisan to use a complimenting cell line to produce Ad24 viral particles having a heterologous-/HIV-encoding nucleic acid within the E1 region. Given the inherent difficulty of propagating viral particles using a complimenting cell line, one skilled in the art would have to invest undue experimentation in order to produce the claimed Ad24 viral particles.

Claim Rejections – 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8, 10-13 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Goosens et al. ("Infection Efficiency of Type 5 Adenoviral Vectors in Synovial Tissue Can Be Enhanced With a Type 16 Fiber" *Arth & Rheum* 2001; 44, 3: 570-577).

Applicants' claims read on a recombinant adenovirus of serotype 24 comprising an E1 deletion or E1 substitution wherein the deletion or substitution prevents replication of the adenovirus. The claims provide for cells and compositions comprising the recombinant adenovirus.

Goosens et al. disclose a recombinant adenovirus having an E1 substitution wherein the E1 substitution comprises a heterologous nucleic acid sequence (i.e. marker protein). Goosen et al.'s recombinant adenovirus is "of serotype 24" in that it comprises an adenovirus type 24 fiber

protein (see p. 571, last 2 paragraphs). Goosens et al. further disclose transforming host cells with their recombinant vector. Based on this disclosure, Goosens et al. anticipates the subject matter of claims 1, 2, 4-8, 10-13 and 15-17.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tmb

Timothy M. Brown
Examiner
Art Unit 1648

James C. Housel 12/12/05

TMB 12/10/05